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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,922	12/21/2001	Nghia H. Chiem	CVZ-003	9904
959	7590	10/02/2003	EXAMINER	
LAHIVE & COCKFIELD 28 STATE STREET BOSTON, MA 02109			SRIVASTAVA, KAILASH C	
			ART UNIT	PAPER NUMBER

1651

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/027,922

Applicant(s)

CHIEM ET AL.

Examiner

Dr. Kailash C. Srivastava

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) Z. 6) ☐ Other:

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Kailash C. Srivastava in Art Unit 1651.
2. Claims 1-43 are pending.

Information Disclosure Statement

3. Applicants' Information Disclosure (i.e., IDS) filed December 24, 2002 as Paper Number 7 has been made of record and considered.

Priority

4. Applicants' claim for domestic priority under 35 U.S.C. §119(e) is acknowledged. Based upon filing of U.S. Provisional Application Numbers 60/3223,962, instant non-provisional U. S. Application Number 10/027,922 is given the benefit of filing date of September 20, 2001.

Claims Objection

5. Claims 4-6 are objected to because of the first recitation of "of Claim" at Line one of each of claims 4-6. Applicants should delete said recitation from each of Claims 4-6.
6. Claim 12 is objected to for the recitation, "multiply and nearly simultaneously or sequentially executed". Term "multiply" should be appropriately corrected.

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 7-8, 18-19, 28, 38 and 42-43 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

- In Claim 7 is recited the limitation, "chromatography step is electrophoresis". There is insufficient antecedence basis for said limitation because said limitation is not recited in Claim 1 from which Claim 7 depends.
- While applicants may be their own lexicographers, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73

USPQ 482 (CCPA 1947). Applicants have used electrophoresis as a type of chromatography. However, each of those terms are distinctly recognized methods in the art. Chromatography is separation of a given chemical/molecule depending upon the absorbance of said molecule to a given resin or material (e.g., paper), whereas electrophoresis is movement of a given material/ particle or molecule under the influence of an electric field (See Webster's Dictionary, Page 238, Column 2, Lines 64-69 and Page 402, Column 1, Lines 47-50). Appropriate correction is requested.

- In Claims 18-19 is recited the limitation, "rate" at which substrate to product enzymatic conversion is affected in presence of a test compound. There is insufficient antecedence basis for said limitation, i.e., rate, because said limitation is not recited in Claim 1 from which Claims 18-19 depend.
- Recitation "concentration" in Claim 28 renders that claim vague, unclear and therefore, indefinite because it is not clear as to concentration of which reaction component is being referred to, the substrate, the enzyme or the products or all of the above or what?
- In Claim 38 is recited the limitation, "altering the rate of said chemical reaction". There is insufficient antecedence basis for said limitation, because said limitation is not recited in Claim 1 from which Claim 38 depends.
- In Claim 42 is recited the limitation, "quenching said chemical reaction". There is insufficient antecedence basis for said limitation, because quenching or stopping the reaction before the step of chromatography is not recited in Claim 1 from which Claim 38 depends.

Other rejected claims depend directly from the rejected claims (e.g., 3) and are, therefore, also rejected under 35 U.S.C. §112, second paragraph for the reasons set forth above.

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of

each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

11. Claims 1-43 are rejected under 35 U.S.C. § 103 (a) as obvious over Dennis et al. (U.S. Patent 5,501,957) in view of Parce et al (U.S. Patent 5,942,443) and Ma et al. (Analytical Chemistry, 2000. Volume 72, Pages 3383-3387).

Dennis et al. teach a two substrate, two-enzyme glycosyltransferase assay method, wherein glycosyltransferase reacts with a donor sugar and an acceptor substrate to form a glycosyltransferase catalyzed product. Subsequently, the glycosyltransferase product as substrate for another transferase, said transferase reacts with a labeled donor sugar material (second compound), wherein as a result of latter reaction, a labeled glycosyltransferase product is produced. The enzyme activity to produce labeled sugar transferase product is the measure for glycosyltransferase activity in the sample. In said reaction the second transferase enzyme has higher affinity to the transferase product than glycosyltransferase has for the acceptor substrate (Abstract, Lines 1-17; Column 3, Lines 18-60 and Claim 1). Thus, Dennis et al. teach a method to assay activity of an enzyme in a two substrate, two-enzyme system. The first step of said reaction system is also a two-substrate one-enzyme reaction. Dennis et al., further teach that the reaction products resulting from said reaction is isolated by any number of conventional techniques (e.g., chromatography or electrophoresis) known in the art (Column 10, Lines 8-14).

Dennis et al., however, do not teach separation of reaction products in a microfluidic device, wherein reaction substrates and products are incubated in an reservoir and are separated in less than 5 minutes in an electrophoretic column that is less than 8 cm long, reactions are performed at different temperatures or the enzyme activity is either enhanced or reduced by reactants. Dennis et al. also do not teach screening for a combinatorial library.

Parce et al. teach a microfluidic device that has multiple channels and reservoirs. Said device has a number of interconnecting reservoirs and channels, wherein channel length of at least one intersecting reservoir and capillary channel system is 5 cm (i.e., below 8 cm) and reaction time of 60 seconds (i.e., = 1min or less than 5 minutes; See Figure 8). Parce et al. further teach assaying the effects of a variety of test compounds on the activity of an enzyme toward the substrate of said enzyme in absence and presence of said test compounds under conditions optimized for said enzyme activity on said substrate, and analyzing for products and substrate concentration as a result of reacting said substrate with said enzyme. The data obtained is applicable to identify inhibitor or enhancers of said enzyme activity amongst the test compounds. Said assays are performed in a microfluidic device, wherein reaction

parameters, e.g., temperature, pH, salt concentrations and electrical field application are controlled (Column 6, Lines 41-59; Column 7, Lines 22-39 and Column 8, Lines 15-29).

Ma et al. teach a method for combinatorial synthesis/ substrate binding through combinatorial screening using 96 capillary array electrophoresis coupled with multiplexed absorption detector (Abstract, Lines 3-14).

One having ordinary skill in the art would have been motivated to modify the teachings from Dennis et al. according to the teachings from Parce et al. and Ma et al. to conduct an assay for enzyme modulators (i.e., enhancers or inhibitors) by conducting enzyme mediated reactions comprising an enzyme, a corresponding substrate for said enzyme and a modulator compound and subsequently quantifying the substrates and products of said reaction via an analytical method (e.g., electrophoresis or chromatography), because each of the cited prior art references teach assaying an enzyme reaction, wherein assay mixture comprises, the substrate, the enzyme and a test compound and subsequently quantifying reactants of said reaction via one of the methods of electrophoresis or chromatography. While Parce et al. remedy the deficiency of a microfluidic device in teachings from Dennis et al., Ma et al. remedy the deficiency of combinatorial screening ~~from teachings of both Dennis et al. and Parce et al.~~

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify teachings from Dennis et al. according to the teachings from Parce et al. and Ma et al. to assay for an enzyme modulator in a microfluidic device through combinatorial screening because examiner cited prior art references teach identification of an enzyme modulator in either two enzyme one substrate or two enzyme two substrate reaction mixture, wherein post-reaction, reactants are analyzed via electrophoresis/chromatography.

From the teachings of the cited references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

None of the prior art references cited above teach the type of substrate (i.e., natural or synthetic), type of bonding of chromophore to substrate, or molecular weight of the test compound in range of 500-2500 or a non-peptide test compound as enzyme modulator. However, the adjustment of particular conventional working conditions (e.g., nature of the compound, type of bonding, molecular weight or chemical type for enzyme modulator) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter, which is well within the purview of the skilled artisan.

Conclusion

12. No Claims are allowed.

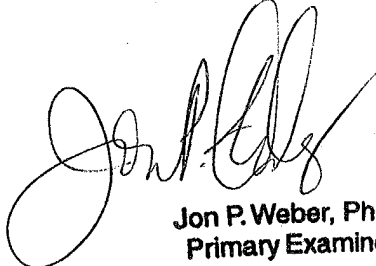
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (703) 605-1196. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Daylight Saving, or Standard time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9306.

Kailash C. Srivastava, Ph.D.
Patent Examiner
Art Unit 1651
(703)-605-1196

September 30, 2003



Jon P. Weber, Ph.D.
Primary Examiner